IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Greene et al. Group No. : 1812

Appl. Serial No.: 08/469,637 Examiner : Pak, M.

Filed: June 6, 1995 Attorney Docket No. : 1488.0710001 (PF172P1)

For: **Human Tumor Necrosis Factor Receptor**

Declaration of John M. Greene and Robert D. Fleischmann Under 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. We, John M. Greene and Robert D. Fleischmann hereby declare and state as follows:

2. We are named inventors of the captioned application, which is assigned to Human Genome Sciences, Inc. (HGS). The work described below was done by ourselves, under our supervision, or as part of a collaborative research effort with other individuals at HGS.

3. As described in each of International application No. PCT/US95/03216, U.S. application Serial No. 08/469,637, and U.S. application Serial No. 08/718,737, we obtained a cDNA clone encoding human Tumor Necrosis Factor Receptor (TNF receptor) by screening a cDNA library derived from early passage human fibroblast HSA 172 cells (*See e.g.*, International application No. PCT/US95/03216, page 6). This clone was designated HSABH13. We have determined nucleotide sequence information for the HSABH13 clone, as described below, using sequencing methods which were routine and publicly available as of the March 15, 1995 filing date of the PCT/US95/03216 application. The HSABH13 clone that we obtained this sequence information from was deposited with the American Type Culture Collection (ATCC) on September 29, 1994 and was assigned ATCC Accession No. 75899 (*See* Attachment A).

4. Evidence that the human HSABH13 cDNA was deposited at the ATCC as Accession No. 75899 is provided in the second column of the IRIS notebook page included herewith as the first page of Attachment B[1]. In one instance, an "X" appears at the end of the HSABH13 clone identifier (see the first column on the notebook page). This HSABH13X designation represents the sequence identifier (SEQ ID) assigned to the sequence information of the first sequencing run. In a second instance, a "P" appears at the end of the same clone identifier. This HSABH13P designation represents the sequence identifier assigned to the sequence information of the second sequencing run. The second column of the notebook page provides two identifying numbers that are assigned by HGS scientists. From looking at the first and second columns together, it is clear that the HGS numbers provided, 195,197 and 1,261,140, represent different sequencing runs performed on the same human cDNA clone, HSABH13. HGS No. 195,197 appears as the identifier on the ATCC-deposit receipt (*See* Attachment A). This indicates that the clone used to obtain the sequence information of HGS No.195,197 was deposited. In other words, even though, as explained below, the data derived from each sequencing run are not identical, the human HSABH13 cDNA clone used to obtain the data from each sequencing run was deposited at the ATCC and assigned Accession No. 75899.

5. The second, third and fourth pages of Attachment B provide data from the IRIS electronic notebook which shows the results from the HSABH13P sequencing run (hereinafter the "second sequencing run") on the human TNF receptor HSABH13 cDNA clone, which has been assigned Accession Number 75899. The nucleotide sequence information obtained from the second sequencing run of cDNA clone HSABH13 differs from that disclosed in Figures 1A and 1B of International application No. PCT/US95/03716 and U.S. application Serial No. 08/469,637, as filed (hereinafter referred to as the "first sequencing run"). The sequence disclosed in the second sequencing run, and the sequence disclosed in the first sequencing run were both obtained from the same HSABH13 clone (Accession No: 75899) using a 373 Automated DNA sequencer (Applied Biosystems, Inc.). Sequencing accuracy using this method is predicted to be greater than 97%.

6. The information obtained from the second sequencing run differs from that of the first sequencing run by including additional flanking regions (nucleotides 1-45 and 1217-1248) and deleting one nucleotide ("C") at position 1076 of the sequence derived from the first sequencing run, resulting in a frameshift for the remainder of the sequence. The amino acid sequence of human TNF receptor deduced from the information obtained in the second sequencing run differs from that deduced from the information obtained in the first sequencing run in that the amino

[1] IRIS is an electronic notebook used by HGS scientists to enter and maintain sequence data.

acids at positions 338-380 of the amino acid sequence deduced from the information obtained in the second sequencing run differ from the amino acids at positions 338-369 of the amino acid sequence deduced from the information obtained in the second sequencing run. This change in amino acids results from the frameshift in the nucleotide sequence described above.

7. The first sequencing run and second sequencing run data share more than 99% identity at the nucleotide level in the TNF receptor coding region, and more than 89% identity at the amino acid level.

8. International application No. PCT/US95/03216 and U.S. application Serial No. 08/469,637 were filed with the sequence data derived from the first sequencing run and U.S. application Serial No. 08/718,737 was filed with the sequence data derived from the second sequencing run.

9. We believe that the actual nucleotide sequence of the human cDNA clone HSABH13 (Accession No. 75899) is the same as that entered in the IRIS notebook for the second sequencing run.

10. We are of the opinion that the correct human TNF receptor nucleotide and amino acid sequences would have been apparent to one skilled in the art in possession of ATCC Deposit No. 75899 and the data from the second sequencing run as of the March 15, 1995 filing date of the PCT/US95/03216 application. This is so because the correct TNF receptor coding sequence can be readily determined from the deposited clone and methods for sequencing this clone were routine in the art in March of 1995.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by find or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereupon.

MARCH 10, 1998
Date

John M. Greene
John M. Greene

Date

Robert D. Fleischmann

COPY

American Type Culture Collection

12301 Parklawn Drive • Rockville, MD 20852 USA • Telephone: (301)231-5520 Telex: 898-055 ATCCNORTH • FAX: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Human Genome Sciences, Inc.
Attention: Craig A. Rosen, Ph.D.
9620 Medical Center Drive
Suite 300
Rockville, MD 20850

Deposited on Behalf of: Human Genome Sciences, Inc.

Identification Reference by Depositor: ATCC Designation

DNA Plasmid, 195,197 75899 PF 172 PCT-US

REDACTED

The deposits were accompanied by: __ a scientific description __ a proposed taxonomic description indicated above.

The deposits were received September 29, 1994 by this International Depository Authority and have been accepted.

AT YOUR REQUEST:

X. We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested October 7, 1994. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Date: October 11, 1994

Annette L. Bade, Director, Patent Depository

cc: Greg Ferraro

Human Genome Sciences, Inc.
Sequence Report
Sorted by Seq ID

Seq ID	HGS	Accde
HSABH13P	1261140	.256
HSABH13X	195197	

HGS

Human Genome Sciences, Inc. (2/4)
Sequence Worksheet
HSABH13P

Sequence Information

HGS Code: 1261140 Sequence ID: HSABH13P

Library Name: HSA 172 Cells

Search Results

Sequence

HSABH13P Length: 1527 Tuesday, March 10, 1998 Check: 830 ..

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   1 CGCCCAGCCG CCGCCTCCAA GCCCCTGAGG TTTCCGGGGA CCACAATGAA
  51 CAAGTTGCTG TGCTGCGCGC TCGTGTTTCT GGACATCTCC ATTAAGTGGA
 101 CCACCCAGGA AACGTTTCCT CCAAAGTACC TTCATTATGA CGAAGAAACC
 151 TCTCATCAGC TGTTGTGTGA CAAATGTCCT CCTGGTACCT ACCTAAAACA
 201 ACACTGTACA GCAAAGTGGA AGACCGTGTG CGCCCCTTGC CCTGACCACT
 251 ACTACACAGA CAGCTGGCAC ACCAGTGACG AGTGTCTATA CTGCAGCCCC
 301 GTGTGCAAGG AGCTGCAGTA CGTCAAGCAG GAGTGCAATC GCACCCACAA
 351 CCGCGTGTGC GAATGCAAGG AAGGGCGCTA CCTTGAGATA GAGTTCTGCT
 401 TGAAACATAG GAGCTGCCCT CCTGGATTTG GAGTGGTGCA AGCTGGAACC
 451 CCAGAGCGAA ATACAGTTTG CAAAAGATGT CCAGATGGGT TCTTCTCAAA
 501 TGAGACGTCA TCTAAAGCAC CCTGTAGAAA ACACACAAAT TGCAGTGTCT
 551 TTGGTCTCCT GCTAACTCAG AAAGGAAATG CAACACACGA CAACATATGT
 601 TCCGGAAACA GTGAATCAAC TCAAAAATGT GGAATAGATG TTACCCTGTG
 651 TGAGGAGGCA TTCTTCAGGT TTGCTGTTCC TACAAAGTTT ACGCCTAACT
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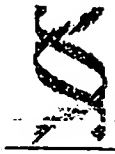

Human Genome Sciences, Inc. (3/4)

Sequence Worksheet

HGS HSABH13P

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 701 GGCTTAGTGT CTTGGTAGAC AATTTGCCTG GCACCAAAGT AAAGGCAGAG
 751 AGTGTAGAGA GGATAAAACG GCAACACAGC TCACAAGAAC AGACTTTCCA
 801 GCTGCTGAAG TTATGGAAAC ATCAAAACAA AGACCAAGAT ATAGTCAAGA
 851 AGATCATCCA AGATATTGAC CTCTGTGAAA ACAGCGTGCA GCGGCACATT
 901 GGACATGCTA ACCTCACCTT CGAGCAGCTT CGTAGCTTGA TGGAAAGCTT
 951 ACCGGGAAAG AAAGTGGGAG CAGAAGACAT TGAAAAAACA ATAAAGGCAT
1001 GCAAACCCAG TGACCAGATC CTGAAGCTGC TCAGTTTGTG GCGAATAAAA
1051 AATGGCGACC AAGACACCTT GAAGGGCCTA ATGCACGCAC TAAAGCACTC
1101 AAAGACGTAC CACTTTCCCA AAACTGTCAC TCAGAGTCTA AAGAAGACCA
1151 TCAGGTTCCT TCACAGCTTC ACAATGTACA AATTGTATCA GAAGTTATTT
1201 TTAGAAATGA TAGGTAACCA GGTCCAATCA GTAAAAATAA GCTGCTTATA
1251 ACTGGAAATG GCCATTGAGC TGTTTCCTCA CAATTGGCGA GATCCCATGG
1301 ATGAGTAAAC TGTTTCTCAG GCACTTGAGG CTTTCAGTGA TATCTTTCTC
1351 ATTACCAGTG ACTAATTTTG CCACAGGGTA CTAAAAGAAA CTATGATGTG
1401 GAGAAAGGAC TAACATCTCC TCCAATAAAC CCCAAATGGT TAATCCAACT
1451 GTCAGATCTG GATCGTTATC TACTGACTAT ATTTTCCCTT ATTACTGCTT
1501 GCAGTAATTC AACTGGAAAA AAAAAAA
```

HGS

Human Genome Sciences, Inc.
Sequence Worksheet
HSABH13P

Sequence Information

HGS Code: 1261140 Sequence ID: HSABH13P

Library Name: HSA 172 Cells Library Catalog: T0039

Search Results

Sequence

DE Murine tumour necrosis factor receptor 2 gene product [Mus musculus]
XX
DT 10-Mar-1998
XX
SQ Sequence 509 BP;
MNKLL CCALVFLDIS IKWTTQETFP PKYLHYDEET SHQLLCDKCP
PGTYLKQHCT AKWKTVCAPC PDHYYTDSWH TSDECLYCSP VCKELQYVKQ ECNRTHNRVC
ECKEGRYLEI EFCLKHRSCP PGFGVVQAGT PERNTVCKRC PDGFFSNETS SKAPCRKHTN
CSVFGLLLTQ KGNATHDNIC SGNSESTQKC GIDVTLCEEA FFRFAVPTKF TPNWLSVLVD
NLPGTKVNAE SVERIKRQHS SQEQTFQLLK LWKHQNKDQD IVKKIIQDID LCENSVQRHI
GHANLTFEQL RSLMESLPGK KVGAEDIEKT IKACKPSDQI LKLLSLWRIK NGDQDTLKGL
MHALKHSKTY HFPKTVTQSL KKTIRFLHSF TMYKLYQKLF LEMIGNQVQS VKISCL*